

Remarks

Reconsideration of the application is urged in view of the amendments above and comments which follow:

The Applicants elect, with traverse, the invention of group VI, which the Examiner has indicated to relate to the use of a Gas6 receptor for the manufacture of a medicament for the treatment of an individual with an elevated risk for a disorder or disease caused by endothelial dysfunction, corresponding to one embodiment of claims 29-31. This is with traverse for two reasons, however. First, Applicants note that in claims 29-31, reference is made to the use of a 'soluble Gas6 receptor', and that this election is made on the assumption that the Examiner had in fact intended to specify this group as relating to the use of a soluble Gas6 receptor.

Second, while it can be acknowledged that the subject matter of group I is patentably distinct from the subject matter of groups II to IX, it is submitted that the subject matter of groups II to IX relate to a common inventive concept. Indeed, these groups encompass claims relating to the use of Gas6 inhibitors in the treatment of endothelial activation or dysfunction. As is clear from the specification, in the context of disease, endothelial activation is considered as a type of dysfunction, i.e. it relates to an unwanted or abnormal activation of endothelial cells. This concept is not disclosed by Avanzi *et al.*. Indeed, Avanzi *et al.* relates to the influence of Gas6 on resting and stimulated Endothelial cells (EC) and indicates that resting ECs produce Gas6 (abstract, right column, lines 6-8). Avanzi *et al.* does not relate to the inhibition of Gas6 or potential therapeutic benefits thereof. To the contrary, Avanzi *et al.* suggests that Gas6 is related to the function of resting EC rather than activated ECs and may function as a 'physiological anti-inflammatory agent' (page 2338, right column, lines 21-22). Thus, Avanzi *et al.* in no way discloses or suggests the inhibition of Gas6 to treat endothelial activation or dysfunction in diseases such as e.g. systemic inflammation. While the "invention" relating to inhibitors of Gas6

e.g. systemic inflammation. While the "invention" relating to inhibitors of Gas6 function which is a soluble Gas6 receptor is elected at this time, it is submitted that Applicants should get the opportunity to rejoin the other types of inhibitors if a generic claim to the treatment of endothelial dysfunction using Gas6 inhibitors is found allowable.

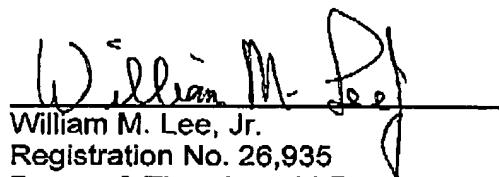
In view of the fact that the claims are presently in the European 'second medical use' format the applicants also replace the claims with new claims 32-44 as a voluntary amendment. The subject matter of these claims corresponds to that in the now-cancelled claims and does not introduce new subject matter. Indeed the claims relating to the treatment of endothelial dysfunction are supported by the description, at least on page 5, lines 26-28 of the PCT publication WO 00/76309. The different disorders to which endothelial dysfunction are known to contribute, and listed in new claims 33-38 are furthermore listed in the section from page 1, line 18, to page 2, line 29 of WO00/76309. Claims 33, 34 and 36, relating to a particular embodiment of the invention which is directed to the treatment and prevention of endothelial activation caused by endotoxins (claim 34), i.e. during surgery (claim 33) such as in sepsis (claim 36) are based on the specification on page 2, lines 15 to 18 of the PCT publication WO 00/76309.

Included in this amendment are both the claim reciting the single inventive concept of the invention (claim 39) and its dependent claims, as well as claims to the alternative embodiments of the invention, which would correspond to one of the other groups (claims 39-44). For the reasons stated above, it is submitted that all new claims should remain and be examined.

In view of the foregoing, it is submitted that the claims of group II-IX should remain in the application and be examined, with only now-cancelled claims 11-20 being withdrawn. The Examiner's further action on the application is therefore awaited.

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Respectfully submitted,



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